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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/557,288	02/27/2006	Mario Tavazza	2520-1068	1741

466 7590 09/22/2008

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EXAMINER	
ZHENG, LI	
ART UNIT	PAPER NUMBER
1638	
MAIL DATE	DELIVERY MODE
09/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/557,288	TAVAZZA ET AL.	
	Examiner	Art Unit	
	LI ZHENG	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-55,58,59,61,63-65 and 68* is/are pending in the application.

4a) Of the above claim(s) *44-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55,58,59,61,63-65 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/17/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 44-55, 58-59, 61, 63-65 and 68 are pending.

Election/Restrictions

2. Applicant's election with traverse of Group III, claims 55-68, C1/A1/AC1 gene and SEQ ID NO: 8 and 9 as well as Begomovirus and Begomovirus TYLCSV as the specie election, cancellation of claims 56-57, 60, 62 and 66-67, and amendments to claims 55, 58-59, 61, 63-65 and 68 in the reply filed on 6/2/2008 are acknowledged.

Applicants contend that the technical feature is the introduction of silent point mutations derived by geminiviruses and distributed in such a way that the length of the regions with contiguous homology between the new mutated sequence and the original one is below or equal to 8 or 5 nucleotides, which is not anticipated by Wezel et al. (response, page 9, 4th paragraph to page 12, 2nd paragraph).

The Office contends that it is the province and duty of the Examiner to say what the technical feature is. Applicants' characterization of what the technical feature is lacks probity. Further, the claim 44 does not recite that the mutation is silent mutation. Still further claims 51-52 in Group II only recite a mutated gene sequence.

Applicants further argue that the method claim for obtaining transgenic plants having long lasting resistance against geminivirus should not be restricted to TYLCSV and SEQ ID NO: 8 an 9 (response, page 12, 3rd paragraph).

The Office contends that the reason for species election is clearly stated in restriction requirement filed 4/1/08. Applicants are reminded that nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute **independent and distinct** inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

Claims 44-54 are withdrawn for being drawn to non-elected invention.

Claims 55, 58-59, 61, 63-65 and 68 including C1/A1/AC1 gene and SEQ ID NO: 8 and 9 are examined on the merits.

The requirement is deemed proper and is therefore made FINAL.

Specification

3. The Abstract is objected to because it is not within the range of 50-150 words.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

4. The specification is objected for the recitation “aminoacid” on pages 8, 13-16, 22-23 and 25. The recitation should be replaced with --amino acid--.

Claim Objections

5. Claim 59 is objected to for the recitation “TYLCSV”. It is suggested to spell out the name of the virus at its first occurrence.

6. Claim 65 is objected to because of the recitation “(SEQ ID No 9)”. It is suggested to rephrase the claim so that the parenthesis is removed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 55, 58-59, 61, 63-65 and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "long lasting resistance" in claim 55 is a relative term which renders the claim indefinite. The term "long lasting resistance" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Further, in claim 55, the last step of the method in instant claims is inconsistent with the preamble. The last step only results in introduction of the vector in any plant, whereas the preamble states that the method is for the preparation of transgenic plant having long lasting resistance against geminiviruses. Adding a selection step is suggested.

Scope of Enablement

8. Claims 55, 58-59, 61, 63-65 and 68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the preparation of transgenic plant having long lasting resistance against geminiviruses by making silent mutations to truncated Rep gene from TYLCSV, does not reasonably provide enablement for making any mutations to truncated Rep gene from TYLCSV having 130 residues from N-terminal of the Rep protein, or any geminivirus-derived sequence encoding an amino acid sequence able to confer resistance against geminiviruses. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are broadly drawn to a method for the preparation of transgenic plant having long lasting resistance against geminiviruses comprising:

a) identification or selection of geminivirus-derived sequence encoding an amino acid sequence able to confer resistance against geminiviruses; b) mutagenesis of the geminivirus gene-derived sequence, wherein the mutations consist of point mutations distributed along the geminivirus gene-derived sequence so that continuous homology between the mutated sequence and the corresponding viral gene sequence is less than or equal to 8 nucleotide; c) insertion of the geminivirus gene sequence mutated in the step (b) in the plant using a construct comprising a plant promoter, a 5' UTR, a geminivirus gene-derived sequence mutagenised according to step (b) and a 3' UTR.

The specification teaches that the proximal 5' region of the C1 gene from TYLCSV in siRNAs population is dramatically under-represented (specification, page 22, lines 14-21). The specification further teaches construction of polynucleotide sequence encoding truncated Rep protein (specification, page 24, table 6). The specification teaches that the first 130 N-terminal amino acid of the Rep protein are enough to inhibit almost completely viral replication in tobacco and tomato while expression of the first 120 N-terminal amino acid has no influence (specification, page 25, lines 30-33; also page 26, line 25 to page 29, line 14). The specification further teaches that construction of a synthetic polynucleotide sequence, modified to be an extremely ineffective target of post-transcriptional gene silencing induced by the infecting virus encoding TYLCSV Rep-210 protein (particularly SEQ ID NO: 4-5, Figure 16B). The specification also teaches the criteria for designing the synthetic polynucleotide sequence (specification, page 30, lines 1-13). The specification further teaches that the

transgenic tobacco plants expressing the synthetic codon modified polynucleotide sequence exhibit a long lasting resistance against TYLVSV (specification, page 32, lines 10-25). The specification finally proposes to obtain transgenic plant with a long lasting resistant against TYLCSV by expressing a synthetic polynucleotide sequence, modified to be an extremely ineffective target of post-transcriptional gene silencing induced by the infecting virus encoding TYLCSV CP protein (particularly SEQ ID NO: 6-7, Figure 22).

The specification fails to provide guidance on how to obtain other geminivirus-derived proteins able to confer resistance against geminiviruses and have similar mode of action as that of truncated Rep protein from TYLCSV. The specification only teaches how to modify a truncated Rep protein, such as Rep-210 or Rep-130 so that the modified truncated Rep protein become an extremely ineffective target of post-transcriptional gene silencing induced by the infecting virus. The specification propose to make similar modification to CP protein of TYLCSV, however, Vanderschuren et al, (2007 Plant Biotechnology Journal 207-220) teach that the resistance mechanism for transgenically expressing CP is largely unknown and that neither transgenic beans expressing the CP of bean golden mosaic virus nor tobacco plants expressing ACMV CP display any resistance (the paragraph bridging pages 209-210). Therefore, without a working example, undue experimentation would have been required for a person skilled in the art to practice the invention with CP genes.

Even for Rep gene from TYLCV, the instant invention only teaches to modify truncated Rep protein, which functions as a dominant negative mutant to

confer resistance to other geminiviruses. Vanderschuren et al, (2007 Plant Biotechnology Journal 207-220) teach that expression of Rep protein was not necessary for resistance by the tomatoes expressing parts of the Rep gene with the intergenic region of TYLCV (page 210, the paragraph bridging left column and right column).

Still further, the specification also fails to provide guidance in terms of how to make modifications other than the silent mutation to generate the claimed genus of variants.

The state of art also teaches that making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al. (1988, Mol. Cell. Biol. 8:1247-1252) teach that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins would have at least 95% identity to the original protein.

Guo et al. (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid

changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2).

Therefore, the instant specification fails to provide guidance for which amino acids of the geminivirus-derived resistance protein can be altered, the type of alteration, and which amino acids must not be changed, to maintain resistant activity.

Without further guidance, undue experimentation would be required for a person skilled in the art to identify other geminivirus-derived sequences encoding polypeptide to confer resistance against geminiviruses, to make any kinds of mutations so that continuous homology between the mutated sequence and the corresponding viral gene sequence is less than or equal to 8 nucleotide, to express the modified protein in plant, and to test whether the transgenic plant show long lasting resistance compare with transgenic plant expressing the wild resistant protein. See *Genentech Inc. v. Novo Nordisk,* A/S (CA FC) 42 USPQ2d 1001 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Therefore, given the claim breadth, lack of further guidance and additional working example, unpredictability of the art, undue experimentation would be required for a person skilled in the art to practice the invention.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claim 55, 58-59, 61, 63 and 68 is/are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Polston et al. (2005, US Patent Application Publication Number 2005/0125862).

The instant claims are drawn to a method for the preparation of transgenic plant having long lasting resistance against geminiviruses comprising: a) identification or selection of geminivirus-derived sequence encoding an amino acid sequence able to confer resistance against geminiviruses; b) mutagenesis of the geminivirus gene-derived sequence, wherein the mutations consist of point mutations distributed along the geminivirus gene-derived sequence so that continuous homology between the mutated sequence and the corresponding viral gene sequence is less than or equal to 8 nucleotide; c) insertion of the geminivirus gene sequence mutated in the step (b) in the plant using a construct comprising a plant promoter, a 5' UTR, a geminivirus gene-derived sequence mutagenised according to step (b) and a 3' UTR; or wherein the geminiviruses

are species of Begomoviruses or TYLCSV; or wherein the gene sequence is truncated C1/AL1/AC1 gene from TYLCSV.

The Office does not give the limitation "long lasting resistance" any patentable weight because it is a relative term with no definite meaning.

Polston et al. teach a method for providing genetically-engineered resistance in plants to TYLCV using a truncated version of the Rep gene of TYLCV (abstract). Polston et al. also teach the TYLCV is a TYLCV-Sordinia (TYLCSV). Polston et al. also teach Rep encoded by C1 gene (paragraph [0008]). Polston et al. also teach introducing silent mutation to achieve codon optimization for optimal expression in host cell (paragraph [0038].

Claims 55, 58-59, 61, 63 and 68 require limitation(s) of generating mutation which has/have a property or characteristic of that mutations consist of point mutations distributed along the geminivirus gene-derived sequence so that continuous homology between the mutated sequence and the corresponding viral gene sequence is less than or equal to 8 nucleotide. Polston et al. teach limitations of making silent mutations as claimed in the instant application but does not mention the characteristic or property of that mutations consist of point mutations distributed along the geminivirus gene-derived sequence so that continuous homology between the mutated sequence and the corresponding viral gene sequence is less than or equal to 8 nucleotide as claimed. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. See *In re Best* 195 USPQ 430, 433 (CCPA 1977). The examiner is not in a position to make a conclusion of

"inherency/anticipation" or "obviousness" since the record does not allow one to determine if and how the claimed subject matter differ from the prior art. Accordingly, the burden shifts to the Applicant to provide evidence that the prior art neither anticipates nor renders obvious the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Li Zheng/

Examiner, Art Unit 1638